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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,982	11/19/2003	Binie V. Lipps	FWLPAT019US	6836

7590 11/16/2006

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EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,982	LIPPS ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/14/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: *Appendix* .

1. Claims 1-23 are currently under prosecution.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-3, 11-12, 15-19, 22-23 are rejected under 35 U.S.C. § 102(b) as being anticipated by US Patent No. 6,294,349, IDS item, as evidenced by Urban, N, Use of Novel Technologies to Identify and Investigate Molecular markers for Ovarian cancer screening and prevention, 1997 Ovarian Cancer Research Program (http://cdmrp.army.mil/scripts/get_item.asp?item=abstract&log_no=OC970002&type=technical)

The claims are drawn to a process comprising bringing together a reagent containing antibodies made against a mixture of proteomic cancer markers with a human saliva sample to form an assay sample and determining whether an immunological reaction has occurred (claim 1), wherein the assay is an ELISA (claim 2) wherein the ELISA results is titer analysis (claim 3), wherein the saliva sample is centrifuged to separate out cells and mucin and collecting the supernatant to form the sample (claim 11), wherein the sample is collected (claim 12), wherein the reagent contains antibodies against a plurality of proteomic markers (claim 15), a non invasive cancer screen comprising obtaining a saliva specimen from a patient, bringing the sample together with a reagent containing antibodies made against a plurality of proteomic markers from different types of cancer cells to

form an assay sample and determining whether a reaction has occurred (claim 16), wherein the assay is an ELISA (claim 17), wherein the assay tests titer (claim 18), wherein results above a predetermined value are indicative of a positive screen (claim 19), a method for monitoring effectiveness of cancer treatment comprising obtaining a first saliva specimen and assaying with ELISA to obtain a first test result, treating the patient and after a period of at least one week, obtaining a second saliva sample, again doing an ELISA and comparing the results of the first and second ELISA to determine effectiveness of cancer treatment (claim 22), wherein a lower titer in the second test is indicative of effective cancer treatment (claim 23).

Urban teaches, in the technical Abstract of Project 2 (page 2 of 3) that p53 and c-erb-2 tumor antigens are markers that are common to a number of different cancers, thus these two markers are both markers from different types of cancer cells.

US Patent No. 6,294,349 teaches a method of diagnosing and monitoring malignant breast carcinomas wherein diagnosis comprises ELISA assay of c-erb-2, CA 15-3 and p53 wherein it is found that higher levels of c-erb-2 and CA 15-3 and lower levels of p53 compared to normal controls is indicative of malignant breast carcinoma (see abstract). In particular, the specification teaches the use of salivary biomarkers to diagnose breast cancer, that is to diagnostically differentiate between women with carcinoma of breast, women with benign tumors and healthy controls (para 2 of Background of the Invention) wherein one or more biomarkers present in saliva are identified. The one or more biomarkers are provided as part of a diagnostic panel for the initial detection, follow-up screening for detection, reoccurrence of breast cancer in women, response to chemotherapy and/or surgical

treatment of the disease state (para 12 of Summary of the Invention) wherein the concentration of endogenously encoded protein is used to diagnose carcinoma of the breast (para 20 of Summary of the Invention). The reference teaches that the saliva samples were taken and frozen until ready for use. The frozen saliva samples were thawed and centrifuged to precipitate cells and mucin in order to extract the bio-marker proteins. The saliva extract was then analyzed for total protein and the panel of biomarkers (para's 9 and 10 of the Detailed Description). C-erb-2 and p53 were analyzed using ELISA kits. The antibodies used in the test do not present cross-reaction with other known tumor markers and the salivary concentrations are substantially above the lower limit of detection for the assay (para 17 of the Detailed Description). It was found that the mean values for CA 15-3 among control groups was approximately 45-50% lower than the mean value for the cancer group (para 24 of the Detailed Description) On the other hand c-erb-2 was not detected in the saliva or the serum of the controls or benign lesions group and conversely the carcinoma group exhibited the presence of c-erb-2 (para 24 of the Detailed Description). Thus the mere presence of c-erb-2 in the sample is the predetermined level that is indicative of a positive screen.

Further, the reference teaches that a saliva test would be useful in the postoperative/post chemotherapy management of cancer patients. Following tumor removal, an expected decrease in marker concentration should follow and eventually plateau to within a normal level indicating that the patient is free of disease. In contrast, a persistently high level of salivary markers may be indicative of tumor recurrence or persistence (para 41 of the Detailed Description). One would immediately envision the elapse of at least a week after first assay before assays for the assessment of response to chemotherapy.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. To the extent that US Patent No. 6,294,349 does not specifically teach that assay reagent contains antibodies made to a mixture of proteomic cancer markers, Claim1-3, 11-12, 15-19, 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,294,349 in view of Urban, N, *Supra.*

The claims are drawn to a process comprising bringing together a reagent containing antibodies made against a mixture of proteomic cancer markers with a human saliva sample to form an assay sample and determining whether an immunological reaction has occurred (claim 1), wherein the assay is an ELISA

(claim 2) wherein the ELISA results is titer analysis(claim 3), wherein the saliva sample is centrifuged to separate out cells and mucin and collecting the supernatant to form the sample (claim 11), wherein the sample is collected (claim 12), wherein the reagent contains antibodies against a plurality of proteomic markers (claim 15), a non invasive cancer screen comprising obtaining a saliva specimen from a patient, bringing the sample together with a reagent containing antibodies made against a plurality of proteomic markers from different types of cancer cells to form an assay sample and determining whether a reaction has occurred (claim 16), wherein the assay is an ELISA (claim 17), wherein the assay tests titer (claim 18), wherein results above a predetermined value are indicative of a positive screen (claim 19), a method for monitoring effectiveness of cancer treatment comprising obtaining a first saliva specimen and assaying with ELISA to obtain a first test result, treating the patient and after a period of at least one week, obtaining a second saliva sample, again doing an ELISA and comparing the results of the first and second ELISA to determine effectiveness of cancer treatment (claim 22), wherein a lower titer in the second test is indicative of effective cancer treatment (claim 23).

Urban teaches, in the technical Abstract of Project 2 (page 2 of 3) that p53 and c-erb-2 tumor antigens are markers that are common to a number of different cancers, thus these two markers are both markers from different types of cancer cells.

US Patent No. 6,294,349 teaches a method of diagnosing and monitoring malignant breast carcinomas wherein diagnosis comprises ELISA assay of c-erb-2, CA 15-3 and p53 wherein it is found that higher levels of c-erb-2 and CA 15-3 and lower levels of p53 compared to normal controls is indicative of malignant breast

carcinoma (see abstract). In particular, the specification teaches the use of salivary biomarkers to diagnose breast cancer, that is to diagnostically differentiate between women with carcinoma of breast, women with benign tumors and healthy controls (para 2 of Background of the Invention) wherein one or more biomarkers present in saliva are identified. The one or more biomarkers are provided as part of a diagnostic panel for the initial detection, follow-up screening for detection, reoccurrence of breast cancer in women, response to chemotherapy and/or surgical treatment of the disease state (para 12 of Summary of the Invention) wherein the concentration of endogenously encoded protein is used to diagnose carcinoma of the breast (para 20 of Summary of the Invention). The reference teaches that the saliva samples were taken and frozen until ready for use. The frozen saliva samples were thawed and centrifuged to precipitate cells and mucin in order to extract the bio-marker proteins. The saliva extract was then analyzed for total protein and the panel of biomarkers (para's 9 and 10 of the Detailed Description). C-erb-2 and p53 were analyzed using ELISA kits. The antibodies used in the test do not present cross-reaction with other known tumor markers and the salivary concentrations are substantially above the lower limit of detection for the assay (para 17 of the Detailed Description). It was found that the mean values for CA 15-3 among control groups was approximately 45-50% lower than the mean value for the cancer group (para 24 of the Detailed Description) On the other hand c-erb-2 was not detected in the saliva or the serum of the controls or benign lesions group and conversely the carcinoma group exhibited the presence of c-erb-2 (para 24 of the Detailed Description). Thus the mere presence of c-erb-2 in the sample is the predetermined level that is indicative of a positive screen.

Further, a saliva test would be useful in the postoperative/post chemotherapy management of cancer patients. Following tumor removal, an expected decrease in marker concentration should follow and eventually plateau to within a normal level indicating that the patient is free of disease. In contrast, a persistently high level of salivary markers may be indicative of tumor recurrence or persistence (para 41 of the Detailed Description). One would immediately envision the elapse of at least a week after first assay before assays for the assessment of response to chemotherapy.

US Patent No. 6,294,349 and Urban teach as set forth above but do not specifically state that the reagent comprises the antibodies against a mixture of proteonic cancer markers in combination.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have combined the antibodies of US Patent No. 6,294,349 together into a single reagent to do a single step assay because US Patent No. 6,294,349 specifically states that the antibodies are useful for diagnosing cancer and because Patent No. 6,294,349 specifically states that the antibodies do not cross react. One would have been motivated to combine the antibodies of Patent No. 6,294,349 into a single reagent in order to save time and expense of doing multiple assays to determine the antigen composition of the saliva.

6. Claims 4-10, 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,294,349 in view of Urban, N, *Supra*, and further in view of Harlow et al (Antibodies, a Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988, p. 142) and Cruse et al (Illustrated Dictionary of Immunology, CRC Press, New York, page 241 , 1995).

The claims are drawn to a process of preparing a reagent comprising at least one proteonic cancer marker comprising providing a colony of cancer cells, extracting at least one proteonic cancer marker from said colony, forming antibodies against said cancer marker and forming the reagent from said antibodies (claim 4), wherein the colony of cancer cells is formed from a publicly available cancer cell line (claim 5), a breast cancer cell line (claim 6), wherein the antibodies are polyclonal antibodies (claim 7), wherein the polyclonal antibodies are produced in animals (claim 8), isolating serum containing said polyclonal antibodies from blood (claim 9), forming the reagent from the serum (claim 10), extracting the proteomic cancer marker from the colony of cells by disrupting the cells, centrifuging the suspension and collecting the supernatant (claim 13), wherein the centrifuging step is done in two states that is separating out cell debris in stage 1 and separating nuclei in stage two (claim 14).

US Patent No. 6,294,349 teaches as set forth above, and further teaches that ELISA kit for assay of c-erbB-2 was purchased from Oncogene Research Company. US Patent No. 6,294,349 teaches as set forth above but does not teach the isolation and production of the antibody to c-erbB-2 used in the saliva diagnostic assay. Further, it is noted that the product sheet for the kit specifically states that the antibodies used in the assay are monoclonal antibodies to the extracellular domain of c-erbB-2 (see Appendix 1).

Urban teaches as set forth above.

Harlow et al teach that monoclonal antibodies are often more time-consuming and costly to prepare than polyclonal antibodies and they are not necessarily the best choice for certain immunochemical techniques. (p. 142).

Cruse et al teach that polyclonal antibodies bind to many different epitopes of an antigen (p. 241).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to prepare polyclonal antibodies to c-erbB-2 using the conventional methods claimed and to substitute those polyclonal antibodies for the monoclonal antibodies against c-erbB-2 of the Oncogene Research Elisa kit because Harlow specifically teaches that monoclonal antibodies are costly to prepare, and thus clearly costly to buy and because Harlow et al specifically teach that they are not necessarily the best choice for certain immunochemical techniques. In particular, since the antibodies of the Oncogene Research Elisa kit are specifically monoclonal antibodies against the extracellular domain of c-erbB-2, one would have been motivated to produce polyclonal antibodies because they are useful for detecting many epitopes, rather than a single epitope of the entire protein, thus many antibodies would bind to the same molecule, producing a strong signal that is easily interpreted. One would have a reasonable expectation of success in producing said antibodies given the well known and conventional nature of polyclonal antibody production. Further, one would be motivated to use, for example, any breast cancer cell line known to express c-erbB-2 as a source material for the colony of cells that are processed to isolate the antigen because cell lines are publicly available for purchase, easy to grow and would provide a ready supply of antigen for production of antibodies.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains,

or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 20-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20-21 are indefinite in the recitation of the phrase "identifying a most highly positive test result". The phrase "most highly positive is a relative phrase which renders the claims indefinite. The phrase is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

9. No claims allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
November 8, 2006

Appendix p. 1

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HER-2/*neu* ELISA

Intended Use

The Oncogene Science HER-2/*neu* ELISA is an *in vitro*, diagnostic device intended for use in the quantitative det HER-2/*neu* in women with metastatic breast cancer who have an initial value of 15 ng/ml or greater HER-2/*neu* v be used in the follow-up and monitoring of patients with metastatic breast cancer. HER-2/*neu* values should be u with information available from clinical and other diagnostic procedures in the management of breast cancer. The serum measurement of HER-2/*neu* as a prognostic indicator for early recurrence and in the management of patie immunotherapy regimens has not been fully established.

Background

The HER-2/*neu* oncogene, also referred to as c-erbB-2, encodes a protein with a molecular weight of 185,000 da belongs to a family of epithelial growth factor receptors structurally related to the Human Epidermal Growth Fact full length p185 HER-2/*neu* protein is composed of a cytoplasmic domain with tyrosine kinase activity, a transmer an extracellular domain (ECD) that is shed from the surface of breast cancer cells [2,3]. Numerous studies have ECD of HER-2/*neu* is a glycoprotein with a molecular weight between 97 and 115kDa and designated p105 [3,4]. accurately quantified in serum with an ELISA [4] that uses monoclonal antibodies [5] that are directed to the exte HER-2/*neu* protein. Many publications show that the ECD is shed into the blood of normal individuals and can be with metastatic breast cancer [4,6-26]. Many of these serum HER-2/*neu* studies have confirmed the substantial c studies that HER-2/*neu* is a marker of poor prognosis, shorter overall survival and biological aggressiveness.

Clinical Utility

Recent scientific studies suggest that quantitation of the ECD may have several important clinical applications su breast cancer patients with metastatic disease [6-10,12,15,17-20,22-26]. These reports have shown that 30-50% positive HER-2/*neu* tumors at primary diagnosis develop elevated levels of serum HER-2/*neu* with progression to cancer [4,6-26]. These studies have also illustrated that monitoring serum ECD levels post-surgery correlated wit disease and that serum HER-2/*neu* levels were observed to increase with disease progression or to decrease wi therapy [12,15,19,20,25,26]. Several reports also show that elevated levels of serum HER-2/*neu* can occur in wo breast cancer that had primary breast tumors that were negative for HER-2/*neu* expression by immunohistochem According to many immunohistochemistry and serum studies, the HER-2/*neu* protein is overexpressed in many t origin including lung [28], prostate [29], pancreatic [30], colon [31], stomach [32], ovarian [33], and hepatocellular

Assay Principle

The Oncogene Science HER-2/*neu* ELISA is a sandwich-type enzyme immunoassay that utilizes two monoclona to the ECD of HER-2/*neu*. (Note: Independent studies have demonstrated that this unique dual monoclonal antib no evidence of interference from Herceptin™ immunotherapy.) The assay quantitates either the full-length molec (p185) or the ECD (p105) in serum, plasma, cell cultures and fluids. The capture antibody has been immobilized surface of microplate wells. To perform the assay, an appropriate volume of specimen is incubated in the coated of the antigen by the capture antibody. The immobilized antigen is then reacted with the detector antiserum. The antibody bound to antigen is measured using a colored reaction product that is quantitated by spectrophotometry amount of *neu* protein in the sample. The Oncogene Science HER-2/*neu* ELISA is completely formulated and off testing format options for end-users.

Patents

Oncogene Science has been granted patents related to quantitation and detection of the ECD p105 domain: (in t #5,401,638, Canada #2,026,250-8, and Europe #0494135) as well as patents related to the quantitation and dete length p185 molecule (in the US, patent #5,604,107 and Europe patent #0412115).

Selected References

1. Coussens, L., et al., Science, 1985. 230: p. 1132-1139.
2. Brandt-Rauf, P., et al., Critical Reviews in Oncogenesis, 1994. 5(2&3): p. 313-329
3. Zabrecky, J.R. et al., Journal of Biological Chemistry, 1991. 266(3): p. 1716-1720.
4. Carney, W.P., et al., Journal of Tumor Marker Oncology, 1991. 6(2): p. 53-72.
5. McKenzie, SJ. et al., 1989. Oncogene 4: 543-548
6. Andersen, T.I., et al., Acta Oncologica, 1995. 34(4): p. 499-504.
7. Watanabe, N., et al., Acta Oncologica, 1994. 33(8): p. 901-904.
8. Molina, R., et al., Anticancer Research, 1996. 16(4B): p. 2295-2300.
9. Molina, R., et al., British Journal of Cancer, 1996. 74: p. 1126-1131.
10. Molina, R., et al., Breast Cancer Research & Treatment, 1998. 51: p. 109-119.
11. Fehm, T., et al., Oncology, 1998. 55: p. 33-38.
12. Isola, J.J., et al., Cancer, 1994. 73(3): p. 652-658.
13. Leitzel, K., et al., Journal of Clinical Oncology, 1995. 13(5). p. 1129-1135.
14. Hayes, D.F., et al., Abstract Presented at the 12th Annual San Antonio Breast Cancer Symposium, 198 1989).
15. Kath, R., et al., Annals of Oncology, 1993. 4: p. 585-590.
16. Yamauchi, H., et al., Journal of Clinical Oncology, 1997. 15(7): p. 2518-2525.

17. Mercer, D.W., et al., Clinical Chemistry, Abstract #846, 1995. 41(S6, part 2): p. S226.
18. Kandl, H., et al., British Journal of Cancer, 1994. 70(4): p 739-742.
19. Narita, T., et al., Breast Cancer Research and Treatment, 1992. 24: p. 97-102.
20. Dia, J., et al., Amer Assoc Clin Chem, 1998. Abstract #208.
21. Krainer, M., et al., Oncology, 1997. 54: p. 475-481.
22. Kynast, B. et al., J. Cancer Res Clin Oncol 119: 249-252, 1993.
23. Takaaski, H. et al. Oncology reports, 1997 Vol 4(2): 349-352.
24. Klein, B. et al., Oncology Report, 1995 Vol 2(5): 759-761.
25. Imoto,S. et al., Jpn J. Clin Oncol, 1999, 29(7): 336-339.
26. Willsher, PC. et al., Breast Cancer Research & Treatment, 1996 40: 251-255.
27. Titus, K., CAP Today, Nov 1999
28. Brandt-Rauf, P. et al., Int. Journal of Cancer, 1994. 56: p. 383-386.
29. Myers, R.B., et al., International Journal Cancer, 1996. 69 (5): p. 398-402.
30. Okada, N., et al., Oncology, 1995. 52: p. 392-396.
31. Wu, J.T., et al., Journal of Clinical Laboratory Analysis, 1993. 7: p. 31-40.
32. Chariyalertsak, S., et al., Tumor Biol, 1994. 15: p. 294-303.
33. Meden, H., et al., Anti Cancer Research, 1997. 17: p. 757-760
34. Luo, J.-C , et al., Medical Science Research, 1993. 21: p. 305-307.

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